

Association of Lower Urinary Tract Symptoms (LUTS) with sexual dysfunction in men aged more than 50 years



A dissertation submitted to The Dr. M.G.R. Medical University, Tamilnadu, in partial
fulfillment of the requirements for M.Ch. Branch-IV (Genitourinary surgery)
examination to be held in August 2014

DEPARTMENT OF UROLOGY
CHRISTIAN MEDICAL COLLEGE, VELLORE

BONAFIDE CERTIFICATE

This is to certify that the work presented in this dissertation titled “**Association of Lower Urinary Tract Symptoms (LUTS) with sexual dysfunction in men aged more than 50 years**” done towards fulfilment of the requirements of the **Tamil Nadu Dr. M.G.R. Medical University, Chennai for the M.Ch (Branch– IV) (Urology)** exams to be conducted in August 2014, is a bonafide work of the candidate **Dr. Chandan Phukan**, Senior Post graduate student in the Department of Urology, Christian Medical College, Vellore under my guidance and supervision. This dissertation has not been submitted, fully or in part to any other board or University.

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“I imagine an author must feel when he writes FTNIS to the plot that, stage by stage has unfolded itself just as he desired to.” Jim Corbett, after annihilating a man eater. These words expressed the deep sense of satisfaction that one experiences after completion of a task done in earnest and with all sincerity. Although completion of a thesis may not be as daunting a task as confronting the jaws of a tiger but nonetheless difficult and impossible to accomplish without guidance, help, and assistance. A lot of hard work has gone into this thesis. And now that it is complete, I feel very much like Mr. Corbett. For this, although I thank everyone who was graciously willing to help, those whom I would particularly like to cite are –

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ABBREVIATIONS

LUTS - Lower urinary tract symptoms

IPSS - International Prostate Symptom Score

IIEF - The International Index of Erectile Function

FSH - Follicle-stimulating hormone.

GNRH – Gonadotropin releasing hormone

LH – Luteinizing Hormone

ED - Erectile dysfunction

TT - Total testosterone

EjD - Ejaculatory disorders

MMAS - Massachusetts Male Aging Study

MSAM -7 - Multinational Survey of the Ageing Male-7

NHSS - The National Health & Social Life Survey

BPH - Benign prostatic hyperplasia

OPD – Outpatient department

INTRODUCTION

Lower urinary tract symptoms (LUTS) and sexual dysfunction are common in the aging male. The association between these two conditions are not yet defined (1,2) . Lately studies using International Prostate Symptom Score, have shown a prevalence rate of Erectile dysfunction (ED) to be >50% in men aged 50 years and above (1).

Traditionally, less attention has been paid to the association between sexual dysfunction and lower urinary tract symptoms. The exact mechanisms via which lower urinary tract symptoms appears to affect sexual function in aging population is still being elusive,

With the growing interest in men`s health, and increased problem of sexual dysfunction this has attracted some attention. LUTS is meticulously evaluated and treated by all, whereas urologists often look into sexual dysfunction in these men.

Presently immense attention has been focused on the same at the international level but there is a paucity in the Indian literature.

India is a developing country with diverse culture, religion, language and attitude. But still faces problems related to unemployment, illiteracy, lack of awareness and mortality due to negligence. Though advancement in health field renders an accessible amount of opportunities to people in treating them still men in India differs a lot from those of men in western countries.

The degree of illiteracy, social taboos and ignorance have made them disinterested in seeking medical treatment. Men in India also have a great difficulty in approaching medical remedies due to their poor socio economic back ground.

With this in mind we designed a study to evaluate the association between Lower Urinary Tract Symptoms (LUTS) and sexual dysfunction.

AIMS AND OBJECTIVES

We performed a case control study to look for the association between Lower Urinary Tract Symptoms (LUTS) and sexual dysfunction in men above 50 years at a tertiary care centre.

Primary objective of the study:

- a) to find the association of Lower urinary tracts symptoms (LUTS) with Sexual dysfunction

Secondary objectives were:

- a) To find the association of severity of LUTS with sexual dysfunction.
- b) Association of co-morbidities with sexual dysfunction

Review of Literature

The 1990s has drawn much attention to gender -based medicine. Extensive research have yielded important findings about health and disease in men. However this knowledge hasn't borne the expected benefits. Men are less conscious than women to seek medical care,. Nearly fifty percent of males are likely to pursue health visits or screening tests when compared to their counterpart (3). Recent data shows nearly 68.6% of men above 20 years of age are obese. As per the data provided by Kung HC et al life expectancy of male trails that of females by 5.3 year (4).

The concept of Men's Health is in its nascent state in comparison to women's. Men's Health is considered by many clinicians to a field concerned with sexual function and prostate. This has recently become a pursued subject in and around world. Millions of dollars are being spent on evaluation of prostate related issues, better urinary flow and improved erections. On the contrary only a negligible amount is being directed to overall improvement of health (5).

Men are more likely to be persuaded to visit their physicians for events such as sports related injuries, alopecia or erectile dysfunction. This presentation to clinician can give an opportunity for a more complete evaluation. In an article published in December, 2005, By Thompson and colleagues (6) confirmed that erectile dysfunction is a primary event which turns out to be a major risk factor for cardiovascular accidents.

Lower urinary tract symptoms (LUTS) –

“Bladder is an unreliable witness” - Bates (1970)

Paul Abrams is the one who coined the term lower urinary tract symptoms. It described symptoms such as prostatism and clinical benign prostatic hyperplasia. This showed that symptoms were due to prostatic pathology and often treated without substantial evidence of underlying cause (7). There was enough evidence by this time that similar symptoms were seen in elderly females and they could not have been attributed to prostatic pathology. There was no evidence that would cite benign prostatic enlargement as the cause of LUTS. Associations could not be shown between either individual symptoms or group of symptoms. The only exception was the association of day time frequency, urgency and urge incontinence with overactivity of the detrusor based on urodynamic study. LUTS described symptoms without describing etiology, as symptoms are neither age, sex nor organ specific (7). For these reasons, the terms ‘voiding’ and ‘storage’ were replaced by irritative and obstructive symptoms. Voiding symptoms can also be due to detrusor underactivity rather than bladder outlet obstruction alone. When evaluating an elderly gentleman one can classify LUTS according to standardized questionnaire depending on its symptoms ranging from mild, moderate and severe lower urinary tract symptoms. LUTS is a combination of symptoms that is attributed to disease that involves lower urinary tract.

The symptoms of lower urinary tract symptoms can be classified as: storage, voiding and post micturition symptoms.

- 1) Storage symptoms are those that are experienced by an individual during the storage phase of the bladder and they manifest as increased frequency during the day, urgency with occasional urinary incontinence and nocturia.
- 2) Voiding urinary symptoms are experienced during the voiding phase of micturition. It includes: decreased in the flow of urinary stream, splitting or spraying of the urinary stream, intermittency, hesitancy, straining to void and terminal dribbling of urine.
- 3) Post micturition symptoms comprises sensation of incomplete voiding and post voidal dribbling.

LUTS have a negative impact on many patients. The level of discomfort vary significantly among individual with the same level of symptom and severity. The lower urinary tract symptoms has a variable impact on the quality of life and is independent of physiological factors. The individual's insight on the severity of the condition and its interference in performing his daily activities may cause embarrassment. This is the principal consideration in one's decision to seek medical treatment.

Benign prostatic hyperplasia (BPH) is one of the most common diseases of aging men. It can be associated with distressing lower urinary tract symptoms (LUTS). Nearly fifty percent of all men who is diagnosed of BPH have moderate to severe degree of LUTS. The primary complaints of the patient is bothersome lower urinary tract symptoms which is manifested as decreased flow of urine, increased urinary frequency, urgency, nocturia, intermittency and sense of incomplete voiding. The

association between BPH and LUTS is complex. Several other conditions in the lower urinary tract and elsewhere may be causative of the symptom complex. Not every patients with lower urinary tract symptoms have prostatic enlargement.

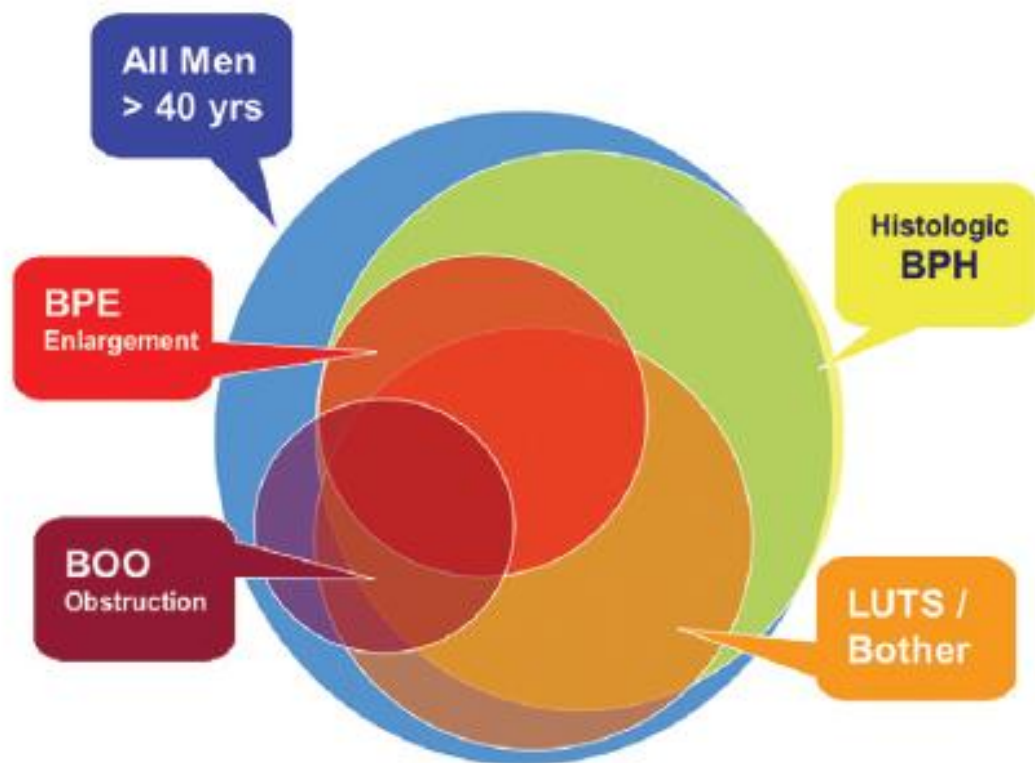


Figure 1: Diagram interpreting the relationship between BPE, BPH, LUTS and BOO (8).

Analytical Epidemiologic Studies of BPH:

Socioeconomic Factors

There is a difference of opinion regarding the effect of socioeconomic factors on BPH. Some have opined higher rates of prostate related surgeries in the affluent class on the other hand others have opined that the BPH related surgery is more in the lower socio economic group. The BACH study have shown that the inability to pay for their health related affairs were the ones with more severe symptoms. (9).

Alcohol and Liver Cirrhosis

Alcohol consumption is likely to inhibit the production of serum testosterone production and its clearance. In spite of this presumed reason for decreased incidence of benign prostatic hyperplasia, studies have shown the opposite result. scrutiny of the PCPT (Prostate Cancer Prevention Trial) demonstrated a protective effect (10) between BPH and alcohol intake.

Essential Hypertension: The sympathetic nervous system through the adrenergic receptors and fibres appears to play a sentinel part in the development of the symptoms of BPH and hypertension. The incidence of LUTS and hypertension is reported to advance with advancing age. To prove an underlying relationship between these two conditions is often difficult. Often the hyperactivity of the autonomic nervous system has been drawn in as a cause for the development of both erectile dysfunction and lower urinary tract systems. However a definite clinical data is missing (11).

Smoking: Smoking seems to enhance the level of both estrogens and testosterone due to the effect of nicotine. This seems to have a positive impact on the

development of benign prostatic hyperplasia. Studies have shown a biphasic relationship between smokers and development of BPH. Moderate smokers were at lesser risk to develop moderate to severe symptoms. On the contrary chain smokers and non smokers were at the same risk for the development of the symptoms. The Olmsted County study have showed that smoking causes decreased flow of urine and development of moderate and severe symptoms. But it didn't show any association with increase in the size of prostate or a rising serum PSA (12).

Physical Activity and the Metabolic Syndrome: There is no substantial evidence that dietary factor plays a part in the development of benign prostatic hyperplasia and lower urinary tract symptoms. The associations between lower urinary tract symptoms, benign prostatic hyperplasia, body mass index and the metabolic syndrome have lately gained immense interest (8). Metabolic syndrome is a condition which compromises dyslipidemia, glucose intolerance, obesity and hypertension that causes an increase in the risk for development of cardiovascular disease. This occurs primarily from risk factors that can be modified such as lack of physical activity and dietary habits. It is more pronounced in the Westernized societies.

Presently evidence suggests a positive association between obesity, physical inactivity, body mass index and the development of both Lower urinary tract symptoms and benign prostatic hyperplasia. Regular physical activity have been shown to have a protective role on the development of metabolic syndrome (13).

Sexual dysfunction: Sexual dysfunction is defined as the failure to enjoy sexual intercourse completely. Sexual dysfunction takes variant forms in males and

females. Man may have a sexual problem if he ejaculates prior to his or his partner's desires, failure experiences delayed ejaculation, is unable to have an erection sufficient for penetration and pleasurable intercourse, painful intercourse, lacks or loses sexual desire.

The International Index of Erectile Function (IIEF) was designed to be available in various languages. It was devised to attend to the needs of various worldwide agencies. It has been accepted as the 'gold standard' to measure the outcome of treatment or clinical trials in erectile dysfunction. IIEF has been in use regardless of the type of treatment involved or population being evaluated. It was recommended by the first International Consultation on Erectile Dysfunction (14), as a tool to measure the outcome of clinical trials for erectile dysfunction. This was, sponsored by the World Health Organization. Ever since its inception in 1997 it has been used to conduct more than 50 trials using various treatment agents different study group.

International Prostate Symptom Score (IPSS): The International Prostate Symptom Score contains eight question (seven symptom related and one QOL, quality of life question) screening tool. This is used to diagnose, identify the symptoms and suggest management. This tool was introduced in 1992 by the American Urological Association. At that time it lacked the 8th question (QOL, quality of life). This was known by the name-AUA -7 (American Urological Association symptom score).

International Prostate Symptom Score has played a fundamental role in the clinical study of lower urinary tract symptoms and benign prostatic hyperplasia.(15)

The IPSS consists of a total score varying from zero to thirty-five points. Those with score of 0 to 7 are grouped into mildly symptomatic group. Those scoring 8 to 19

classified into moderately symptomatic. Finally those scoring more than 20 are categorised as severely symptomatic. This has become an integral part of not only epidemiologic studies but also treatment studies. The accessibility of this scale in validated translations in various languages allows comparison across various cultural group.

Relevant anatomy and physiology of lower urinary tract in males:

Bladder muscular and mucosal arrangement:

The urinary bladder is divided structurally into 3 parts: supratrigonal, trigonal and bladder neck. The supra trigonal part of bladder is mainly composed mainly of randomly arranged fibres of the detrusor with overlying urothelium. The supratrigonal region is a seven cell layers thick with a loose underlying lamina propria below it which allows for bladder distension on filling.

The trigonal region is bounded by the two ureteric orifice and internal urethral meatus. The epithelium is only 3 cell layer thick in this region. It has a dense and thick lamina propria, which is attached tightly to underlying muscle. The muscles in trigonal area have well defined layers. The inner most layer is continuation of the inner ureteric muscles forming superficial trigonal muscle. The deep trigonal muscle layer is formed by the continuation of Waldeyer's sheath. The outermost layer is continuation of detrusor muscle and is arranged in inner circular and outer longitudinal layers.

Bladder neck in male involves continuation of muscles from the trigonal region (16)
The superficial trigonal muscle layer continues till the verumontanum. Deep trigonal

muscle ends at the bladder neck. Continuation of outer circular muscle from trigonal region along with the fibromuscular part of prostate, forms ring like structure in the bladder neck region. The longitudinal detrusor muscle fibers, which are posteriorly placed, continue at bladder neck in ring like fashion and form an effective bladder neck sphincter.

Bladder Circulation:

Arterial supply: Superior and inferior vesical arteries arise from anterior branch of internal iliac artery and reach bladder via lateral and posterior pedicle respectively. There can be some direct branches from the internal iliac artery apart from the named ones.

Venous drainage: Small veins draining bladder form vesical plexus, which also receives blood from the dorsal penile vein in males. This plexus drains into the internal iliac vein.

Lymphatic drainage is mainly to external iliac group of nodes via perivesical channels and nodes. Anterior and lateral part may get drained directly to obturator and internal iliac group of nodes. The bladder base and trigonal region drains into the internal iliac and common iliac group of nodes.

Bladder innervation:

Bladder is supplied by autonomic nerves, both sympathetic and parasympathetic. Efferent fibers reach bladder via lateral and posterior pedicles through pelvic plexus. Sympathetic supply has its origin in thoracolumbar segment and reaches pelvic plexus by the superior hypogastric plexus and nerves. Parasympathetic efferent originate in sacral segment and reach bladder via pelvic plexus. Parasympathetic

efferent is mainly responsible for detrusor contractions. The bladder neck area has adrenergic innervation that is responsible for bladder neck sphincter contraction. The sympathetic innervation to the detrusor though sparse is thought to be responsible for detrusor muscle relaxation. The afferent fibers travel in both sympathetic and parasympathetic fibers.

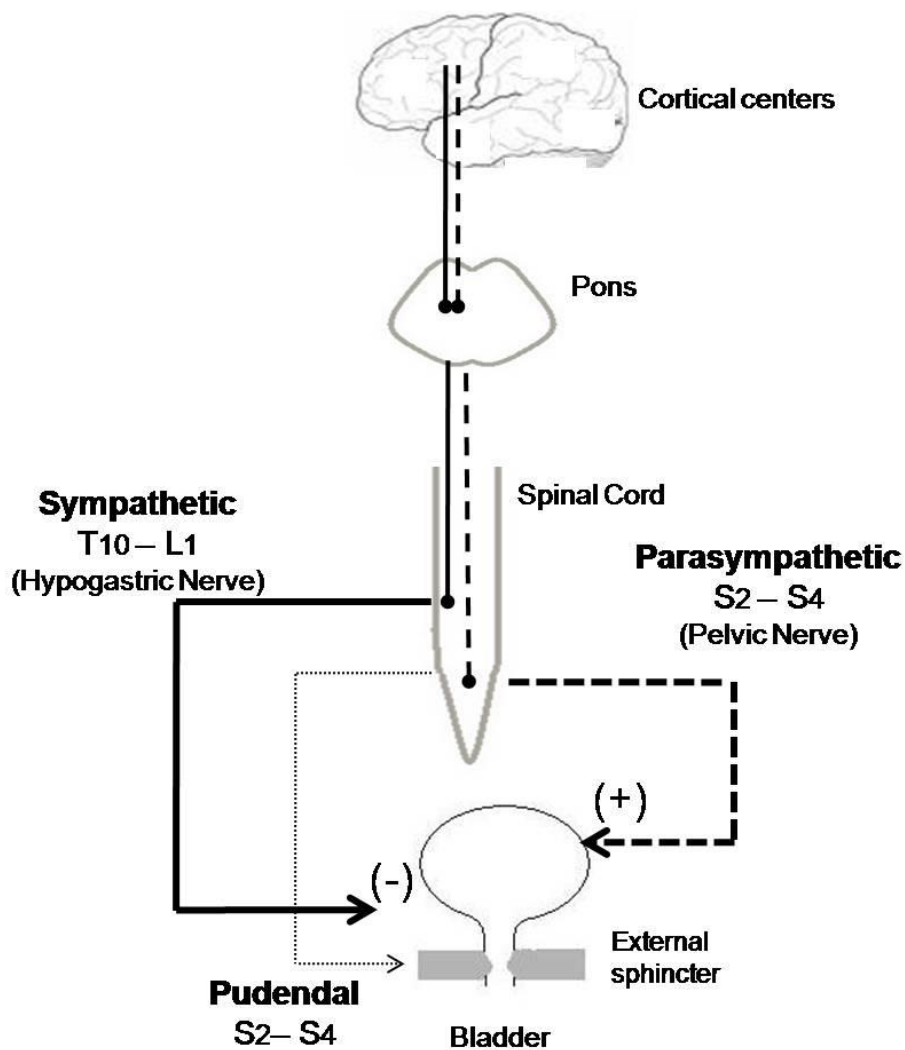


Figure 2: Bladder Neuronal innervations

Prostate

Anatomical considerations

Prostate is an ovoid structure which extends from bladder base to the membranous urethra. Prostate is bounded by a capsule which is more prominent posteriorly and laterally. It is composed of elastin, collagen and smooth muscle fibers. Denonvillers' fascia is located posterior to the prostate. There are smooth muscle fibers which transverse from the prostatic capsule to the Denonvillers fascia, and an areolar tissue layer is placed between the rectum and Denonvillers. Anteriorly and laterally it is covered by visceral endopelvic fascia which also covers the periprostatic venous plexus. Laterally pubococcygeal part of levator ani with its parietal endopelvic fascia surrounds it. The pelvic fascia is thickened at place where prostatic visceral and parietal endopelvic fascia covering levator ani meets forming arcus tendineus fascia pelvis. The cavernosal nerves maintain a postero-lateral relationship to prostate and are invested by the parietal pelvic fascia. Apex of prostate continues with the striated sphincter. Microscopically some prostatic glands can be seen invading the striated muscle of the sphincter. Prostatic urethra runs through it. Urethra is lined by transitional epithelium and is closer to the anterior surface. Prostatic urethra angulates anteriorly at midpoint. The angulation is approximately 35 degrees, can vary from 0-90 degrees. The proximal part of prostate before angulation (preprostatic urethra) has preprostatic sphincter (bladder neck) in males and periurethral glands drain into it. Prostatic urethra receives glandular secretions from peripheral part of prostate, ejaculatory ducts and utricle at verumontanum. Transitional zone glands drain at the junction of preprostatic and prostatic urethra. The glands of central zone drain into the ejaculatory ducts and are probably derived embryologically from urogenital sinus. These two parts of prostatic urethra differ in function also (17). Anterior fibromuscular stroma forms the anterior portion of prostate. It is devoid of glandular structures and extends from bladder neck to the striated sphincter.

Prostatic circulation:

Arterial supply of prostate: Mainly by the inferior vesical artery. Inferior vesical artery divides into urethral branch and capsular branch. Urethral branches penetrate the prostate at its base and run parallel to the prostatic urethra caudally. Most of the branches lie from 1-5 o' clock position and 7-11 o' clock position. These urethra branches mainly supply transitional zone and periurethral zone glands. Capsular branches also run posterolaterally with cavernosal nerves and pierce the capsule to run perpendicularly to supply the peripheral zone.

Venous drainage: Periprostatic venous plexus is responsible for venous drainage of the prostate. The dorsal vein and perivesical venous plexus is in continuity with periprostatic venous plexus and they drain into the internal iliac vein.

Lymphatic drainage –into internal iliac nodes and the obturator nodes mainly. Some drainage occurs into the presacral group and external iliac group of nodes.

Prostatic innervation:

Sympathetic and parasympathetic nerve supply of prostate arise from thoraco-dorsal and sacral nerve roots respectively. Sympathetic nerves are responsible for the contraction of smooth muscles of prostate including the bladder neck and the parasympathetic nerves stimulate glandular secretions. Afferent nerves also travel along them and can be blocked at the base of prostate during the prostatic biopsy.

Membranous urethra:

Anatomy

Membranous urethra spans from the apex of prostate to the bulbar urethra and is on an average 2.5 cm long. It is surrounded by a striated sphincter which is omega shaped. It is thinnest posteriorly as most of its fibers splay laterally. Most of striated sphincter is composed of type 1 muscle fibers, which are of the slow twitch type and can contract for long time. Somatic supply to the sphincter is via pudendal nerve and some branches from the pelvic plexus travel above the levator ani to reach sphincter. Autonomic supply is probably via cavernosal nerves, however their significance in maintaining continence is not known. Not much is known about the afferent nerve supply. The mechanisms necessary in maintaining continence in males include, mucosal folds which coapt during contraction to form a watertight seal, the submucosal tissue and the connective tissue including the puboprostatic ligaments and suspensory ligaments, smooth muscles at bladder neck and smooth and skeletal muscles of striated sphincter and pubococcygeal muscle of levator ani.

Physiology of Lower urinary tracts

The lower urinary tract functions can be summarized as: reservoir of urine at low pressure, maintenance of continence and voluntary periodic complete expulsion of urine at low pressures. These occurs in two phases: the storage phase and the voiding phase.

Storage phase:

Bladder should stores urine at low pressure during the storage phase with appropriate sensations without overactivity. The bladder matrix is mainly composed of elastin and collagen. Elasticity and viscoelasticity are partly responsible for normal bladder compliance. Various neuronal mechanisms also plays a role in maintaining low pressure storage during the filling phase. Sympathetic nerves cause contraction

of bladder neck by stimulating alpha 1 receptors predominantly present at bladder neck thus maintaining continence. Excitation of Beta 3 receptors present on detrusor smooth muscles is proposed to relax the bladder musculature during filling phase. Increased afferent activity in the pudendal nerve during the storage phase may inhibit the effector neurons which supply the detrusor muscle. It has been proposed that urothelium release of some inhibitory mediators which causes relaxation of detrusor smooth muscle.

Voiding Phase:

Voiding is result of coordinated neural activity. It is initiated at cortex and coordinated at micturition centre located at pons in the midbrain. Voiding is initiated when the sensation of bladder filling reaches the threshold to initiate a micturition reflex. The inhibited is maintained by the centre at midbrain and sacral parasympathetic outflow via the pelvic nerve. Parasympathetic outflow causes coordinated detrusor smooth muscle contraction that results in bladder emptying. Funneling of bladder neck is seen when vesical pressure increases above the proximal urethral pressure. The contraction of longitudinal smooth muscle during voiding causes shortening and widening of the proximal urethra.

Sensations of filling and distension normally occur during filling phase and are responsible for initiating micturition, whereas sensation of urgency and pain are pathological. Most of this afferent activity travels in pelvic nerves and enter spinal cord at sacral level (18).

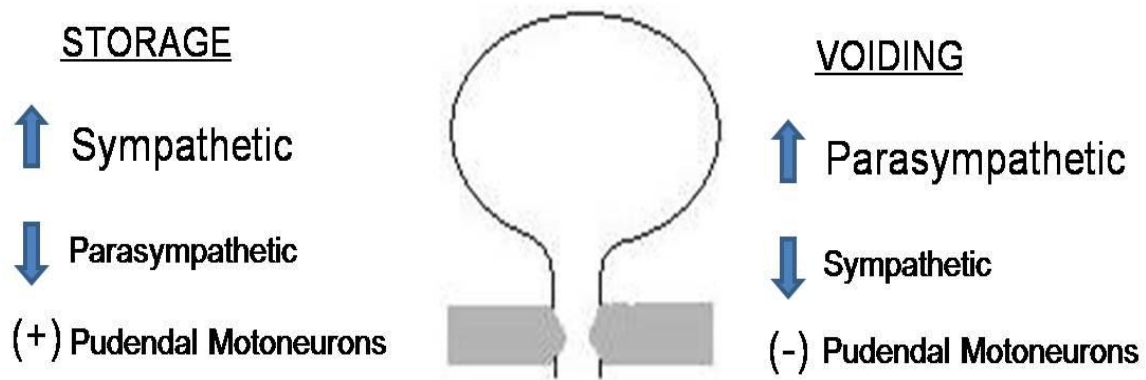


Figure 3: Neural activity during voiding and storage phases

LUTS and sexual dysfunction: The association between lower urinary tract symptoms and erectile dysfunction has come into limelight recently because both diseases are not only highly prevalent but also occur in the same age group in males. This association bears significantly to the overall quality of life. The Cologne study of Germany performed a survey of 4489 men in the age between 30–80 years. A self-administered questionnaire was used and found the prevalence of lower urinary tract symptoms was found to be around 72% in men with erectile dysfunction, whereas it was 38% in men without erectile dysfunction³. They further found an increase in the prevalence of erectile dysfunction in older age groups. This was noticed irrespective of the presence of LUTS in the above mentioned group. The presence of erectile dysfunction was also significantly associated amongst individuals who had undergone a pelvic surgery, and in those who had co morbidities like hypertension and diabetes mellitus.

The Cross National Study was a community based study which was undertaken to find the prevalence of erectile dysfunction in Malaysia, Japan, Italy and Brazil (19). They interviewed 2400 men (~ 600 per country). This interview was done using a standardised questionnaire. They defined erectile dysfunction as the “failure to attain as well as maintain an erection satisfactory for sexual intercourse”. For their study they classified men into various groups based on their reply to could achieve a satisfactory erection:

- a. No erectile dysfunction : if the reply was “always”,
- b. Mild ED when the reply was -Usual
- c. Moderate ED when the reply was - sometimes
- d. Complete ED when the reply was -never.

They found that prevalence of erectile dysfunction increased with the increase in age and this was uniformly seen in all the four mentioned countries.. The study also found a association between lower urinary tract symptoms and erectile dysfunction. This study further found an association between erectile dysfunction and other factors such as smoking, diabetes, coronary artery disease and depression. The incidence of erectile dysfunction was found as Brazil (15%), Italy (17%), Japan (34%) and Malaysia (22%) (19). One of the most notable risk factors for erectile dysfunction was age. Men in the age group 50-60 years were two times more likely to develop erectile dysfunction while comparing to men in the age group 40-50 years. This risk for the development of erectile dysfunction increased by five times for men in the age group 60-70years (20). Similar to erectile dysfunction, the prevalence of benign enlargement of the prostate also increases from eight percent in the fourth to more than eighty in the eighth decade (15). A cross-sectional evaluation of the association between sexual function and lower urinary tract

symptoms in a survey noted that sexual satisfaction inversely correlated with increasing age and lower urinary tract symptoms (21). The risk of erectile dysfunction increased with the severity of LUTS, and this association was greater than known risk factors (eg. coronary artery disease, respiratory problems and smoking). This further highlights that ED is an important aspect to enquire in patients who present with LUTS (22).

The Epidemiologia de la Disfuncion Erectile Masculina (EDEM) survey: A study of 2476 men from Spain in the age group 25–70 years. It was a community based study. Interview was conducted at home. They had to answer a self-administered questionnaire (23). The prevalence of erectile dysfunction in this group was 18.9%. This was based on the erectile function subgroup of the International Index of Erectile Function. There was significant correlation between the ageing of the patient and risk of development of erectile dysfunction.. The study also detected other risk factors that were associated with erectile dysfunction such as the presence of prostatic ailments, diabetes mellitus, essential hypertension, peripheral vascular disease, coronary artery disease, pulmonary disease, rheumatism and allergy. A correlation was found between the severity of lower urinary tract symptoms according to the IPSS scale and the possibility of erectile dysfunction. After adjusting for age the odds ratio for the development of erectile dysfunction was calculated. It showed the OR to be 2.39 in those with moderate symptoms but it increased in the group with severe symptoms to 6.47.

The Alf-One study included nearly 3000 male with lower urinary tract symptoms from five countries. The study also showed that one of the major risk factors for the development of ejaculatory and erectile dysfunction was the presence of lower urinary tract symptoms preceded by aging (24). The Alf-One study was similar with

the findings of the Multinational Survey of the Ageing Male survey. The Alf-One study found that the risks of erectile dysfunction and ejaculatory dysfunction are double in men with severe lower urinary tract symptoms than those without severe lower urinary tract symptoms. They further found that the patients with severe lower urinary tract symptoms had six times the risk for development of painful ejaculation. Abnormal erectile and ejaculatory responses have a considerable adverse effect on the QoL (quality of life) in those men who were sexually active previously. This causes significantly increased levels of anxiety and depression in these people (25). Hence the preservation of sexual function in the aging male is a vital component of the quality of life.

The largest study conducted to till date is the (Multinational Survey of the Aging Male) MSAM-7 survey. This study was conducted on an international scale and was designed to evaluate the association between lower urinary tract symptoms with sexual function in a detailed and meticulous fashion (1). In contrast to previous studies that concentrated mainly on the assessment of erectile dysfunction, the MSAM-7 survey incorporated evaluation of all domains of sexual activity. It not only studied on the aspects of ejaculatory dysfunction (EjD) but also on the impact of lower urinary tract symptoms on the QOL (quality of life). The questionnaires were sent to more than 14,000 men in the age group 50–80 years. This study included the populations of seven countries (France, Italy, United Kingdom, Germany, America, Spain and the Netherlands which possessed different customs and life style. The incidence of erectile dysfunction increased gradually and considerably with the severity of lower urinary tract symptoms ($p < 0.001$). They found the prevalence of severe lower urinary tract symptoms -82.5% , moderate - 65.8% whereas mild LUTS was 43%. Aging led to an increase in the erectile dysfunction (p

< 0:001). The association between severity of lower urinary tract symptoms and erectile dysfunction was seen inspite of the presence of co morbidities (hyperlipidemia, hypertension, diabetes mellitus and cardiac disease). There was a strong association between the severity of lower urinary tract symptoms and of both erectile and ejaculatory dysfunction. Among men presenting with diabetes mellitus or hypertension, a greater prevalence of erectile or ejaculatory dysfunction was seen when compared with men without these conditions. The associatin between sexual dysfunction and severity of lower urinary tract symptoms remained apparent in each age group. The approximate percentage of patients with lower urinary tract symptoms who wanted medical interventions for their condition was only 19% in the MSAM-7 survey. This suggested a lack of motivation or enthusiasm among these groups to visit their physicians. Increased awareness is required in these elderly male patients to diagnose lower urinary tract symptoms due to their ignorance. Those with moderate or severe lower urinary tract symptoms should be meticulously enquired regarding both erectile and ejaculatory function. Reliable and validated investigative tools are available to rule out the sexual dysfunctions in male genders . The extensive accessibility of treatments for erectile dysfunction may help these group of patients to discuss issues of sexual dysfunction confidentially with their doctors. The disadvantages associated with some of the treatments options available for benign prostatic hyperplasia, including effects on sexual function, should be informed to the patients and their relatives in well in advance. Many epidemiological trials have shown that erectile dysfunction is strongly linked to the severity of lower urinary tract symptoms and is not dependent on age or coronary artery diseases (26–28).

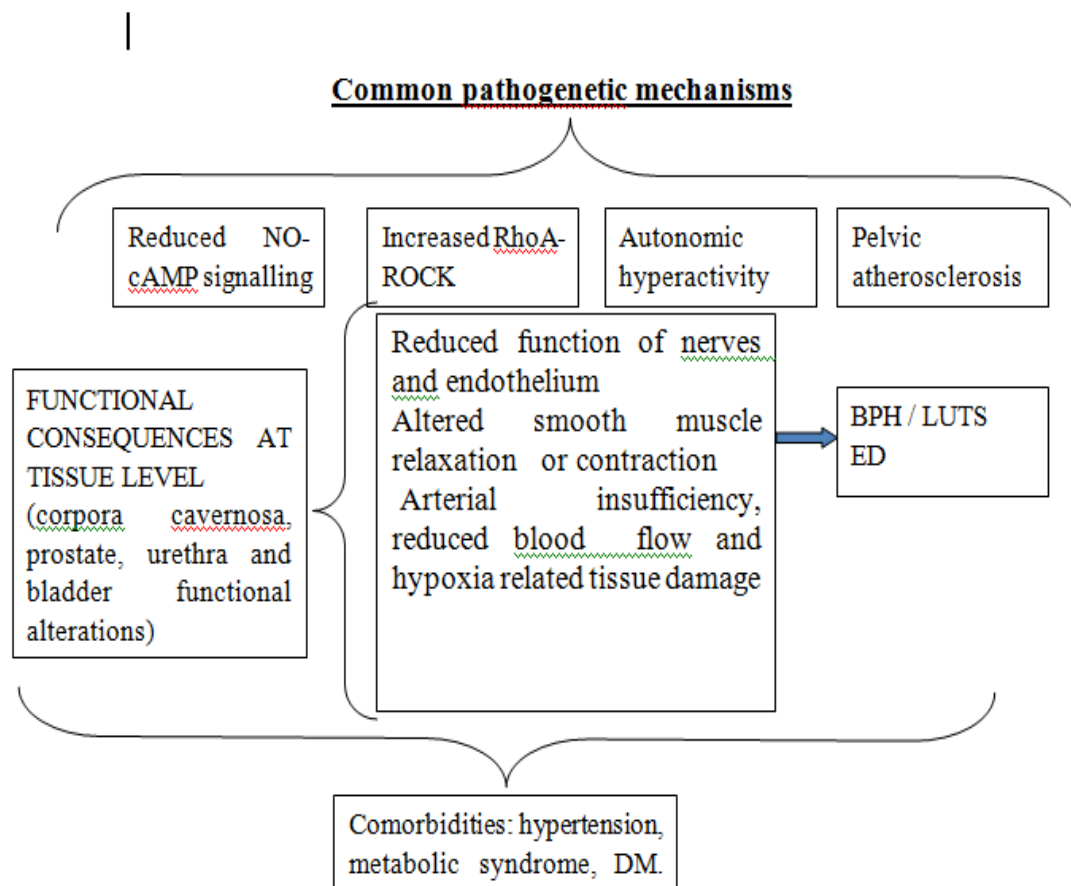


Figure 4: Diagram showing the various pathogenic mechanism

The mechanisms for the association of erectile dysfunction and Lower urinary tract symptoms is not yet defined. Various theories have been proposed which includes:

- 1) The pathway involving the (NOcGMP) Nitric oxide–cyclic guanosine monophosphate
- 2) Enhancement of (ROCK) RhoA–Rho-kinase signalling,
- 3) Hyperactivity of the autonomic nervous system
- 4) Atherosclerosis of the pelvic vessels.

1. The pathway involving the (NOcGMP) Nitric oxide–cyclic guanosine monophosphate: This pathway conducts the activity of regulating relaxation of

smooth muscle in penis and erection has been well characterised (29). Evidence exists, for NO which plays a major role in the regulation of smooth muscle tone of bladder, prostate, and urethra (30). Release of nitric oxide activates a process which leads to formation of cGMP. This leads to decrease in the level of intracellular calcium whereby causing relaxation of smooth muscles. Protein such as cGMP- specific protein kinase are enhanced. Two types of NO synthase (NOS)- neuronal NOS (nNOS) and endothelial NOS (eNOS) have been seen in the in the tissues of corpora cavernosum. The role of nitric oxide in prostate related lower urinary tract symptoms have been studied in vivo on cultured prostate, urinary bladder and urethral smooth muscle.(31) These findings from such study may help one to understand the mechanism which is caused by decrease in the generation of nitric oxide. This leads to gradual deterioration of nerves and the overlying epithelium. Studies have shown that essential hypertension and the metabolic syndrome also has an association with the lower urinary tract symptoms and erectile dysfunction. (32).

2. The mechanism of RhoA/Rho-kinase:

The smooth muscle tone is maintained through dual mechanism –

a) Calcium-dependent pathway

b) RhoA–ROCK calcium-sensitising pathway. Activation of RhoA–ROCK pathway causes decrease in the smooth muscle relaxation resulting in erectile dysfunction and LUTS. In a similar manner the RhoA–ROCK signalling in the penile tissue was seen to be increased in conditions such as diabetes mellitus. This process is exaggerated in conditions associated with erectile dysfunction. An increase in the signal of muscarinic receptor causes activation of the Rho A pathway which causes involuntary bladder contractions.(33,34).

3. Hyperactivity of the autonomic nervous system :

Autonomic hyperactivity is a nervous stimulation that causes exaggeration of parasympathetic and sympathetic system. It is known that the α -adrenoceptor system plays an important role in the pathophysiology of ED and LUTS secondary to BPH (35) with increased sympathetic activity. Various α 1-adrenergic receptors present in prostate, urinary bladder and penile tissue mediates the tone of the vessels and the smooth muscles (36). In an animal study using rats where the rats were fed with a fatty diet. This study revealed that the rats developed hyperglycaemia and increased resistance of insulin along with increase in the proliferation of cells. These led to increased contraction of the α receptors and α -adrenoceptor-mediated contraction and progress of benign prostatic hyperplasia(37). These along with other pathways like advanced end results of glycation, reactivation of oxygen species probably affect both lower urinary tract symptoms and erectile dysfunction.

4. Atherosclerosis of the pelvic vessels:

Development of atherosclerosis of urinary bladder, genitalia and prostate is the harbinger to all of the above described theories. The development of pelvic atherosclerosis causes reduction of signals for nitric oxide and upregulation of the RhoA/ROCK pathway. It also acts as a component of the autonomic hyper activity and metabolic syndrome. The possibility of acquiring risks for erectile dysfunction and atherosclerosis, like hypertension and diabetes mellitus, can also affect lower urinary tract symptoms and benign prostatic hyperplasia (38,39). Age and sexual function has a strong bondage and the younger population were more sexually activity. (40). A study comprising of 2801 men in the age group 17 to

93 years revealed, 5% with impotence in age group 50-59, compared to which 35% in the age group 70-79 and 59% in more than 80 years. In a survey conducted with 2801 men in private practice aged between 17 to 93 years revealed, 5% of men in their 50s with impotence, in comparison with 35% in their 70s and 59% in their 80s (41).

A study conducted in 2011 in France randomly selected men in the age group 50 – 80 years (21). They concluded that not only the desire for intercourse but also frequency of sexual activity was found to be linked with age ($p < 0.001$), involving erectile and ejaculatory function. It was also evident that men with lower urinary tract symptoms were more likely to suffer with sexually dissatisfaction than those without symptoms. The possibility of having sexual dissatisfaction appeared to increase with the severity of lower urinary tract symptoms (21).

Aging impairs the progressive function of the hypothalamic-pituitary-gonadal axis. In male, this gradual deterioration shows a significant difference in the age of onset, rapidity and intensity of the decline between the individual. The above syndrome is known as ADAM (androgen decline in the aging male), LOH (late-onset hypogonadism), or TDS (testosterone deficiency syndrome).

Hypogonadism in men, is clinically characterised by a reduced concentration of serum testosterone, where patients present with various signs and symptoms. This includes erectile dysfunction, decreased libido, decreased in the amount of ejaculate, loss of hair of the face and body, lethargy, decreased lean body mass, decreased bone density, increased body fat, fatiguability and anaemia (42,43). Hypogonadism in adult men is often given less importance because in spite of the presence of associated symptoms, these men are often ignorant of their symptoms.

Very often they attribute these symptoms to miscellaneous causes, including ageing (42). The total testosterone (TT) has not been used as a standard criteria for defining hypogonadism as the cut off level for the normal concentration of serum testosterone is not defined (44). Hypogonadism has been defined by Vermeulen as less than 319 ng/dl i.e two and half standard deviations less than the mean normal total testosterone in young individuals (45). Testosterone level less than 300 ng/dl is associated with decreased bone mineral density (43). Others have defined hypogonadism as total serum testosterone less than 325 ng/dl (44).

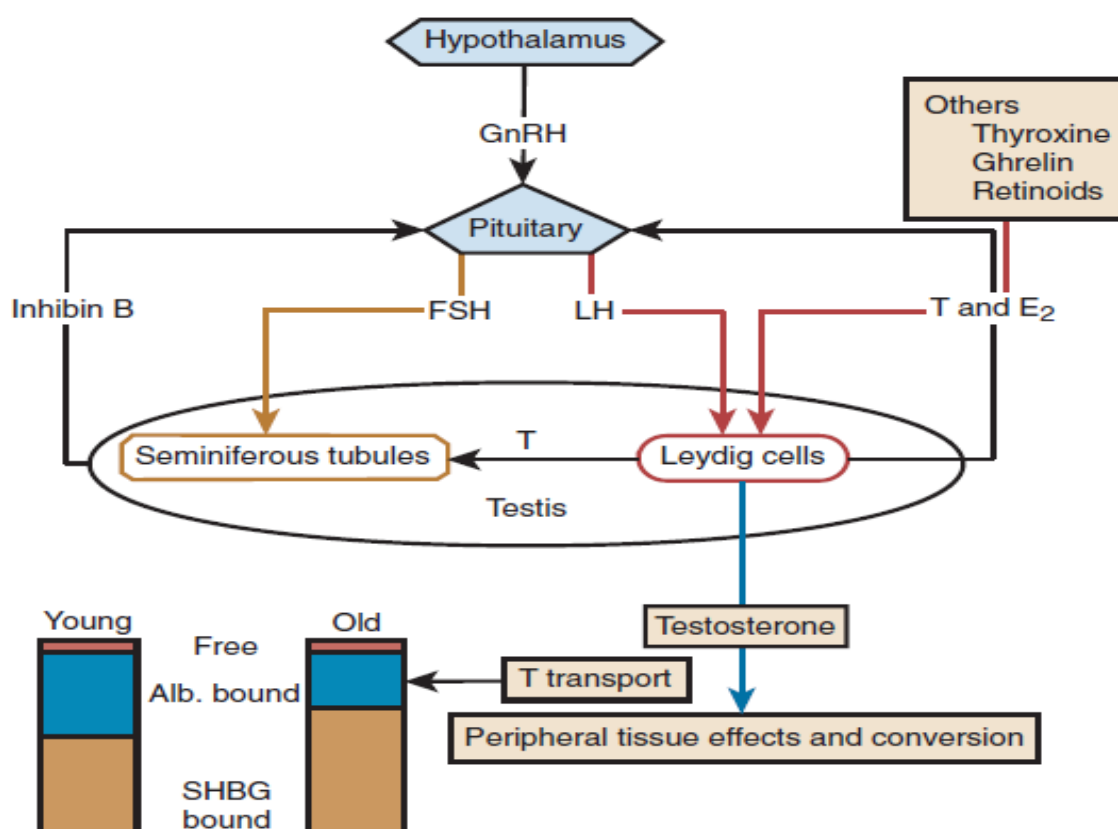


Figure 5: showing the effect of age on the production, transport and metabolism of testosterone (T).

The figure depicts that the LH (Luteinizing hormone) plays an important role on the regulation of testosterone production. With the gradual onset of aging of the pituitary

and hypothalamus causes decrease in the production of GNRH (gonadotropin-releasing hormone) and LH (LuteinizingHormone). Only 2 % of the testosterone either circulates, rest is protein such as SHBG (sex hormone binding globulin) or albumin. With the onset of agint the production of sex hormone binding globulin increases. Bioavailable testosterone becomes activated and gets converted to other hormones like (estradiol (E2), dihydrotestosterone, dehydroepiandrosterone). FSH, follicle-stimulating hormone.

Materials and methods

This was a prospective study done at the Urology department of a tertiary care hospital, for a period of one year from August 2012 to July 2013.

It was approved by the institutional review board, (Institutional research board no: 8069/6.8.2012).

Inclusion criteria:

Males more than 50 years attending the LUTS clinic were included as the case group (LUTS) and matched patients without LUTS were enrolled as the control group (No LUTS).

Exclusion criteria:

Those who were on medical therapy for lower urinary tract symptoms, patients with penile deformity, and pre existing diagnosis of erectile dysfunction and depression (who was evaluated using PRIME- MD questionnaire) were excluded from the study.

All these patients were interviewed by the primary observer after obtaining consent.

All base line data recorded the client's status about demography, socioeconomic status, Anti social activities like substance abuse (smoking, alcohol), co morbidities (Type 2 DM, hypertension, chronic renal failure, heart diseases) and medical history. They underwent a physical examination (height, weight, pulse rate, blood pressure, examination of the external genitalia and a digital rectal examination) and blood investigations was done for glucose, lipid profile, creatinine and serum testosterone. An uroflowmetry with post void residual urine was performed on them.

To objectively evaluate the severity of LUTS, the International Prostate Symptom Score (IPSS) and to evaluate sexual dysfunction, the International Index of Erectile Function-15 questionnaire was administered. The International index of the erectile function is the gold standard measure of the sexual function in males. This tool is being used in many trials for erectile dysfunction (46). The Primary Care Evaluation of Mental Disorders screening questionnaire for depressive symptoms (PRIME-MD) was used as a instrument to assess psychosocial health and depression (47). When the patient was found to be suffering from depression he was excluded from the study. Later the results of the IPSS, PRIME-MD questionnaire, IIEF-15 and their correlation with lower urinary tract symptoms were statistically analyzed. Uroflow rates diagnostic implications and limitations

Uroflowmetry is a noninvasive first line screening test for individuals who have lower urinary tract symptoms. It gives quantitative and objective information that can help in understanding the etiology of lower urinary tract dysfunction.

There are some prerequisites for a uroflowmetry. Privacy should be provided during the test. Instruction to void should be given when the individual has a normal urge to void. Artifacts must be taken into account when recording the values of uroflowmetry. Patients' frequency volume chart values must be compared with results of uroflowmetry to know if these values represent his day to day normal voids. Patient should be asked if the void is representative of his normal day to day void.

What does a normal uroflow represent? Normal uroflow has a smooth bell shaped (arc-shaped) graph. The gentle curves rather than rapid changes in amplitude are the function of detrusor function which is a smooth muscle and does not show rapid variations.

Factors that result in deviation from normal pattern of flow rate: Decrease in detrusor contractility can result in a smooth curve of lower amplitude. Similarly, compressive obstruction with increased urethral opening pressure due to benign prostatic hyperplasia shows a flattened asymmetric curve with slowly declining part. Constrictive obstruction resulting in reduced lumen (e.g. stricture) size produces a plateau like flow curve.

Rapid changes in flow rates may result due to variety of causes. Variations in driving force such straining, rapid changes in outlet resistance such as contraction or relaxation of striated sphincter or pelvic floor, urethral compression or interference at meatus can all result in rapid changes in flow rates. Any artifact that causes interference in urinary stream from meatus to the flowmeter can potentially cause rapid fluctuation in flow rates e.g. movement of stream across the surface of funnel or movement of patient.

Factors other than detrusor contraction and bladder outlet resistance that affect the uroflow are voided volume and technical considerations. Maximum flow rates (Q_{max}) depends on voided volume. Small volumes (< 150 ml) and large voided volumes (.500ml) may be the reason for low Q_{max} . Technical specifications for measuring flow rates have been standardized by International Continence Society (48).

LUTS was determined by IPSS. IPSS, a validated eight-questionnaire scale for assessing LUTS. It is based on factors like decrease in the flow of urine, incomplete voiding, increased frequency, urgency, straining to void and nocturia. The first seven questions have responses that ranges from 0 to 5, resulting in an overall score of 0 to 35. Symptoms were grouped as absent when the IPSS score was less than zero. It was grouped as mild when the score was less than or equal to seven,

moderate when the score was between 8 to 19 and severe when the score was more than or equal to 20. The eighth question was used to assess Quality of Life. The response ranged from 0 to 6.

Sexual dysfunction was assessed using the International Index of Erectile Function (IIEF) by Rosen and colleagues. The IIEF contains 15 questions that quantify five domains of sexual function— sexual desire, erectile function, intercourse satisfaction, orgasmic function and overall satisfaction. It is the most widely used questionnaire . This has been useful to clinicians in day to day clinical practice specifically for the evaluation of erectile dysfunction. The instrument classifies ED severity into five categories: No ED (22 to 25), mild (17 to 21), mild to moderate (12 to 16), moderate (8 to 11) and severe (5 to 7). It is 15 questions, standardized scale for evaluation of male sexual function that examines separate domains of Erectile Function (1 to 5,15), Intercourse Satisfaction (6 to 8), Orgasmic Function (9-10), Sexual Desire (11-12), Overall Satisfaction (13,14).

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To assess their psychosocial health the Primary Care Evaluation of Mental Disorders screening questionnaire for depressive symptoms (PRIME-MD) instrument was given to the case group. It has 2 components, the first is a patients self-administered questionnaire. The second component is used by the physician for the individuals who test positive to the first set. (47). They are scored as:

- a) less than 4 - no treatment warranted
- b) 5-15 – intermediate , treatment based on the impairment of function
- c) >15 - warrants treatment eg antidepressant, psychotherapy.

The cut off values of the variables.

The normal values of the blood tests was compared with the laboratory values at the institution.

Serum creatinine

> 1.4mg % was considered as chronic kidney disease.

Blood sugar values

Fasting blood sugar = 70-100mg%,

Glucose 2 hr post food < 140mg%.)

Lipid profile:

Total cholesterol < 160mg%

HDL - 40-60mg%

LDL - < 100mg%

Serum triglyceride < 150mg%.

Normal blood pressure according to JNC 7 is less than 120/80mmHg.

A testosterone level of 212-755 ng/dl is the laboratory reference range for the institution laboratory. A value less than 212 ng/dl was considered as low. In such patients the free and bioavailable testosterone levels was calculated.

Statistical analysis: These two groups were compared using Stata 10. Univariate analysis was done by 1) Chi square and 2) Two sample Mann – Whitney U test.

Multivariate regression analysis using logistic regression for dichotomous variables was performed.

The **sample size** was calculated based on a power of 90% and assuming the prevalence of sexual dysfunction in men more than 50 years with lower urinary tract symptoms to be 49% (1). A sample size of 134 was calculated for both the arms. The association of lower urinary tract symptoms and sexual function scores were calculated not only for the total sample but also in both the groups, age cohort (fifty to fifty-nine years, sixty to sixty nine and more than seventy years). The presence of various co morbidities (hypertension, coronary artery disease, diabetes, hyperlipidemia). In addition the relationship to addictions such as tobacco chewing and consumption of alcohol with the primary variable. The association of body mass index (BMI) and total cholesterol levels with sexual dysfunction was also evaluated

Study design: It was a case control study.

The formula used to calculate the sample size was-

$$n = \frac{(Z_{\alpha} + Z_{\beta})^2 * (p_1 q_1 + p_2 q_2)}{d^2}$$

Where,

Z_{α} = Z value for α level (1.96 at 5% level)

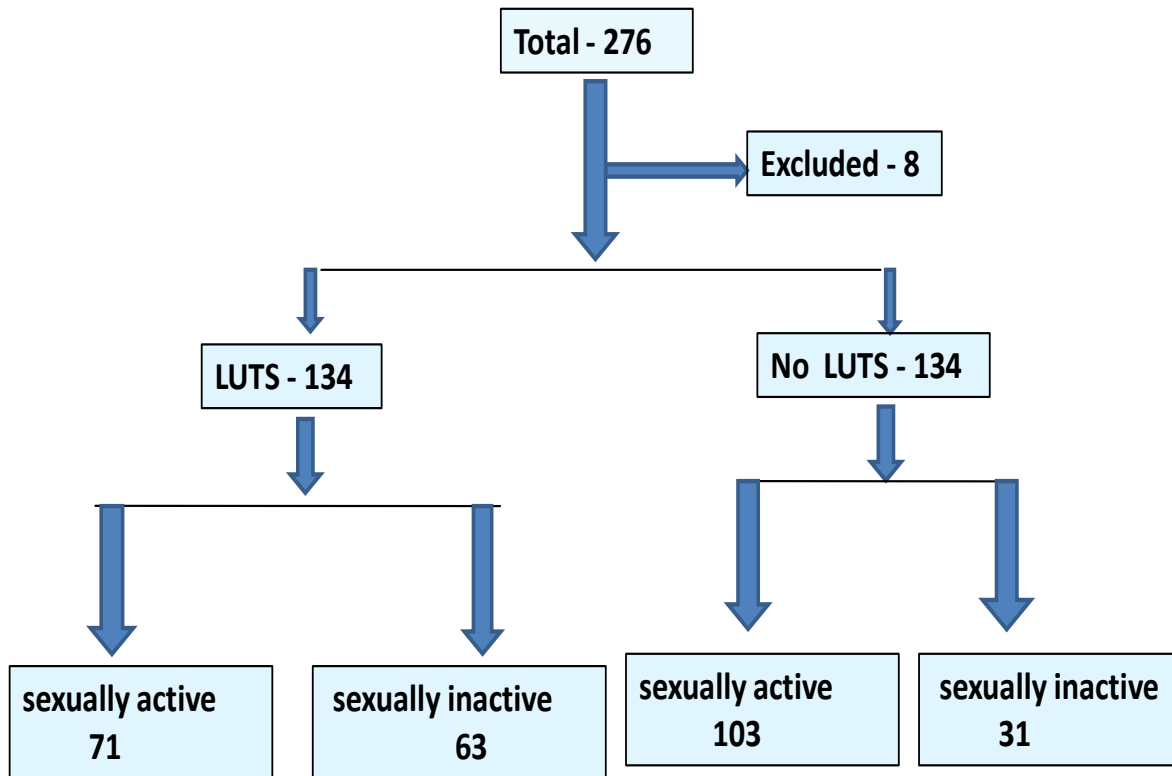
Z_{β} = Z value for β level (1.28 at 10% level)

p_1 = Prevalence in first group; $q_1 = 1 - p_1$

p_2 = Prevalence in Second group; $q_2 = 1 - p_2$

d = clinically meaningful difference between two groups.

Results and observations



Christian Medical College, Vellore

Figure 6: Consort diagram showing the distribution of groups

Out of 276 consecutive patients who attended the urology OPD, eight patients were excluded. There were 134 patients in both the arms. 71 patients were sexually active in the LUTS group whereas 103 were active in the no LUTS group.

Demographic profile

		LUTS (n = 134)	No LUTS (n = 134)	p value
Age	50-59	60(45%)	83(62%)	0.014
	60-69	55(41%)	41(31%)	
	>70	19(4%)	10(7%)	
Co- morbidities	DM + Hypertension	17(13%)	22(16%)	0.687
	DM	19(14%)	21(16%)	
	Hypertension	20(14%)	15(11%)	
	No co morbidities	78(58%)	76(53%)	
Addictions	Smoking	68(51%)	42(31%)	0.37
	Alcohol	4(3%)	5(4%)	0.86

Table 1 : table showing the demographic profile in both the groups

The age was not matched in both the groups but this was adjusted by taking age adjusted multivariate analysis. Both the groups were all matched for their co morbid conditions (presence of both diabetes mellitus and hypertension, diabetes and hypertension alone or addictions).

		LUTS (n = 134)	No LUTS (n = 134)	p value
Education	Uneducated	3(2%)	3(2%)	0.647
	Upto 10 th	44(33%)	35(26%)	
	11 – 12 th	39(29%)	40(30%)	
	Graduate and above	48(36%)	56(42%)	
Married		126(94%)	132(99%)	0.149

Table 2 : table showing the education and the marital status in both the groups

Both the groups were well matched for the education status. In evidence the presence of a partner, and the level of education had similar effect in both the groups.

Lower urinary tract symptoms versus sexual activity

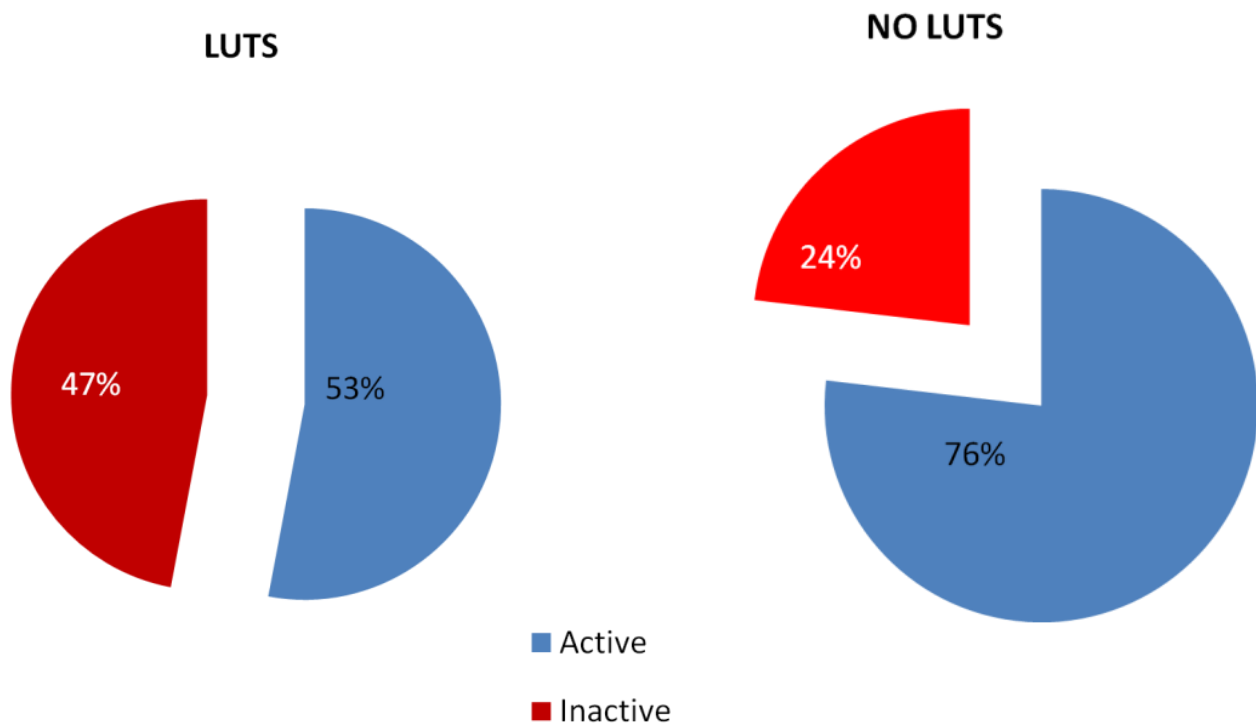


Diagram 3: Pie diagram showing sexual activity in both the groups

As shown in the pie diagram 76% of men in the No LUTS group were sexually active when compared to 53% in the LUTS group and this was statistically significant ($p=0.001$)

Age versus sexual activity

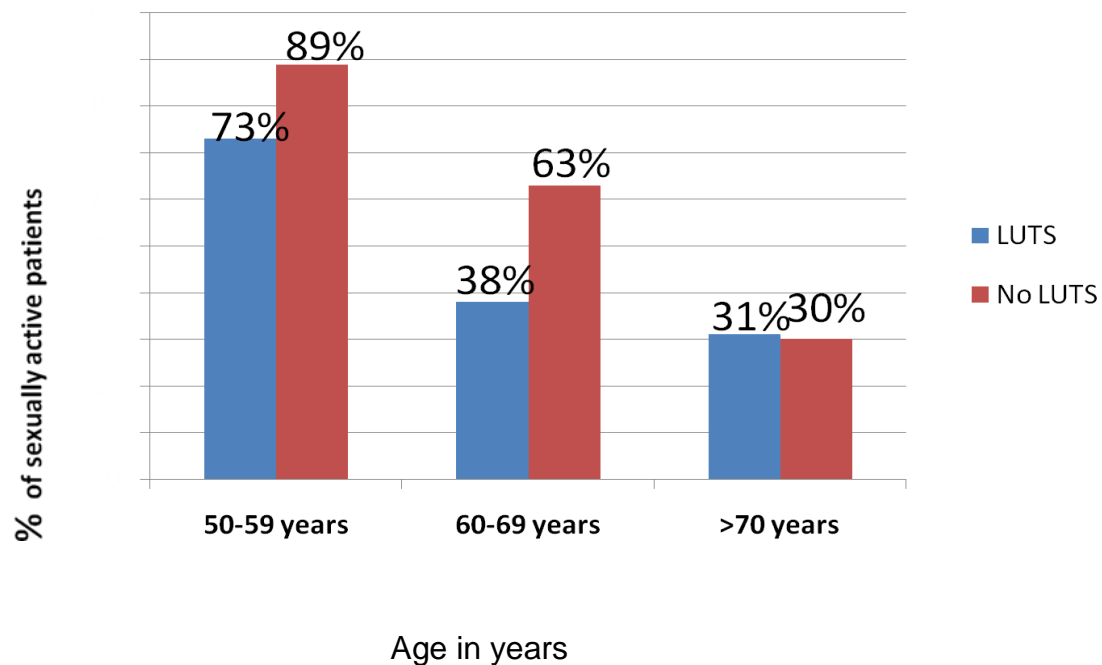


Diagram 4: showing Age versus sexual activity

The bar diagram showing the age in years versus the sexual activity. As expected the sexual activity decreases with age. But the maximal affect of the decline in sexual activity was seen in the younger group, aged 50-70 years, with lower urinary tract symptoms (LUTS). This was also statistically significant ($p=0.001$)

Sexual function (IIEF-15) versus LUTS

	LUTS (n=71) Median (IQR)	No LUTS (n=103) Median (IQR)	p value
Erectile function	23 (17 - 24)	24 (20-25)	0.05
Orgasmic function	8 (8 – 9)	8 (7 – 8)	0.41
Sexual desire	7 (6 – 8)	8 (7 – 8)	0.009
Intercourse satisfaction	10(7 - 10)	10 (9 – 12)	0.001
Overall satisfaction	8 (6 – 8)	8 (7 – 8)	0.017

Table 5: Showing the components of IIEF vs. LUTS

As shown in the above table Lower urinary tract symptoms had a significant impact on the erectile function, sexual desire, intercourse satisfaction and also overall satisfaction of the IIEF- 15.

According to Rosen et al (1) an IIEF score of less than 14 is considered to have erectile dysfunction (ED).

An age adjusted multivariate analysis was done to see the effect of age, LUTS, co morbidities (presence of diabetes mellitus, hypertension), hyper cholesterolemia and serum testosterone effect on the erectile function. As shown in table 6 Lower urinary tract symptoms continued to be a significant factor affecting the erectile function. Though hypercholesterolemia was a significant factor affecting the erectile function, the multivariate analysis didn't review it. S. testosterone less than 212ng/ml

was taken as cut off value and an age adjusted multivariate analysis was taken to see the effect of testosterone on the erectile function. It was concluded that there was no significant effect of serum testosterone on the erectile function.

Risk factors		Age adjusted OR (95%CI)	p value	Multivariate OR (95%CI)	p value
Age	50-59			1	
	60-69			5.94 (3.1-11.5)	<0.001
	>70			10.5 (3.9-28.6)	<0.001
LUTS		2.75 (1.5-4.9)	0.001	2.96 (1.6-5.5)	0.001
BMI	<20	1.63 (0.9-3.1)	0.04	1.76 (0.9-3.5)	0.10
	20-25	3.29 (1.1-10.2)	0.12	3.87 (1.1-13.2)	0.03
	>25	1		1	
DM		1.67 (0.9-3.1)	0.09	2.04 (1.0-4.1)	0.06
Hypertension		1.19 (0.6-2.2)	0.57	1.07 (0.05-2.2)	0.85
Hypercholesterolemia		0.50 (0.3-0.9)	0.02	0.57 (0.3-1.1)	0.08
Testosterone		0.82 (0.3-2.4)	0.72	0.59 (0.2-1.9)	0.38

Table 6: Showing prevalence of risk factors for erectile dysfunction

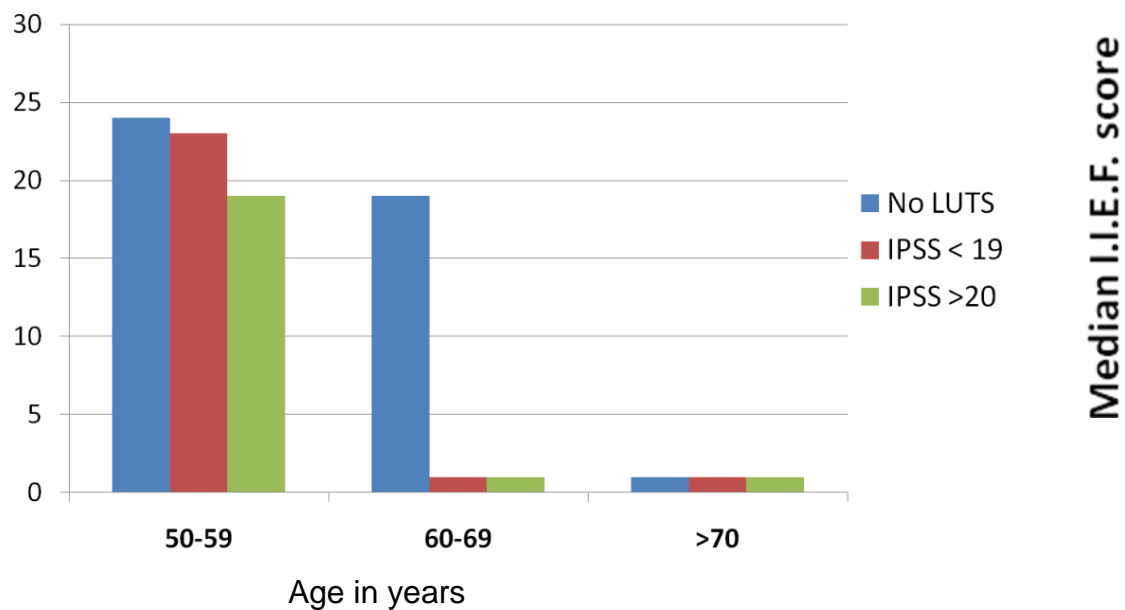


Diagram 7 showing: Erectile dysfunction vs. Severity of LUTS and age group

An attempt was made to find the association between the severity of lower urinary tract symptoms and the erectile function. As shown in the diagram 7, median IIEF score for erectile function was plotted against the severity of LUTS and age group. Severity of LUTS was classified as IPSS score less than 19 and more than 20. It was seen that the maximum effect of severity of lower urinary tract symptoms on the erectile function was seen in the age group 60- 70 years.

Age (years)	LUTS Median (IQR)	No LUTS Median (IQR)
50-59	378 (292 - 500)	338 (283 – 451)
60-69	396 (311 – 502)	340 (278 – 421)
>70	445 (288 – 572)	353 (331 – 391)

Table 8: showing the median testosterone values

The median testosterone value in both the groups were around 350ng/ml. This also shows the average testosterone value in the elderly Indians.

When enquired into the reason of not being sexually active, more than 50% of the patients cited due to the presence of LUTS as a rational behind it . Whereas those in the no LUTS group cited various religious belief and age to be the factor for being sexually inactive

	LUTS (n=63)	No LUTS (n=31)
LUTS	39	0
Religious belief	8	10
Age	9	11
Joint family	1	0
Spousal/partner factor	3	7
Unmarried	3	3

Table 9: showing the reason for not being sexually active

Discussion

Lower urinary tract symptoms (LUTS) and sexual dysfunction are common problem of the aging population. This is the first study evaluating Indian patients with lower urinary tract symptoms and sexual dysfunction. The study showed that sexual activity is commoner in the aging men. When enquired they replied that there was an increased level of anxiety in association with these problems.

Our study found a strong association between lower urinary tract system and sexual dysfunction. This was also showed by the study by Rosen et al (1) and Diokno et al (49). We used standardised and validated scales for measurement of lower urinary tract symptoms and sexual dysfunction. These scales were administered by the principal investigator in all cases. The incidence of sexual dysfunction with lower urinary tract symptoms 47% in the present study. This is well comparable to the prevalence of 49% (46) in the western literature by Rosen et al (1). But unlike the study by Rosen which was multinational community based with questionnaires being mailed to the people, this was single institution based and the performa were filled by the primary investigator.

Age is considered as an important risk factors for the development of erectile dysfunction. In comparison to men in the age group 50-60 have twice the risk for development of erectile dysfunction in comparison to men in the age group 40-50 years. This risk further rises five times for men in the age group 60-70 years.

Numerous community-based surveys (1,11,46,49) have shown that the age of the men considered for a study accounts for difference in the prevalence of erectile dysfunction and lower urinary tracts symptoms. The National Health & Social Life Survey found that lower urinary tract symptoms is a major risk factor for

development of erectile dysfunction. An odds ratio (OR) of 3.13 was seen in 1410 men in the age group 18–59 yr (46). The Krimpen survey while evaluating men more than 50 years of age found that the presence of severe ejaculatory and erectile dysfunction to be 10 times higher in men in the aged more than 70 years in comparison to the 50–54 yr of age Using logistic regression This study using logistic regression further demonstrated the odds ratio to be 7.5 in the association between severe LUTS and ED. The odds ratio was 4.2 between severe LUTS and ejaculatory dysfunction (50).

The present study showed that men without lower urinary tract symptoms were significantly more sexually active. It showed about 50% of male with LUTS were sexually inactive whereas only 24% of men without LUTS were sexually inactive, this was statistically significant ($p=0.001$). This could possibly be due to the lack of effective primary care in India and the consequent delayed management of LUTS. Earlier detection and optimization of the general health and lower urinary tract symptoms may significantly improve men's health in the country.

The exact pathway of sexual dysfunction in men with LUTS is not well understood. Various literature have proposed three common pathophysiologic mechanisms (11) :

- 1) The change in the NO(nitric oxide) pathway in the prostate
- 2) Atherosclerosis of pelvic vessels
- 3) Hyperactivity of the autonomic nervous system.

It is proposed that risk factors for erectile dysfunction such as diabetes mellitus, smoking, dyslipidaemia and hypertension reduces the activity of NOS (nitric oxide synthase) in prostate and bladder. This causes reduction in NO level. Evidence for this hypothesis can be derived from studies in humans (26) and animal models (30) .

Hyperactivity of the autonomic nervous system most likely plays a direct role in altered voiding and erectile function (46).

Lastly, atherosclerosis which is a common cause of erectile dysfunction, could result in reduced perfusion of the urinary bladder and an associated increase in smooth muscle cell proliferation and contractility thereby leading to lower urinary tract symptoms (51).

The Baltimore Longitudinal study of ageing men found a strong association between Benign prostatic hypertrophy (BPH), obesity and diabetes mellitus (52). Our study showed most of the patients in both the LUTS and no LUTS groups to be in the acceptable BMI range. There was no association between LUTS, obesity and co morbid conditions like DM, hypertension. This was similar to the finding of Rosen et al (1) which showed that the association between sexual dysfunction and lower urinary tract symptoms is not dependent on co morbidities such as hypertension diabetes mellitus, coronary artery disease and hypercholesterolemia.

The various components of the sexual dysfunction in the International Index of erectile function-15 (sexual desire, erectile and orgasmic function, intercourse and overall satisfaction) was significantly associated in the patients with LUTS which correlated well with the MSAM (Multinational Study of the Aging Male-7) study (1).

When enquired about the reason of not being sexually active the majority of patients in the LUTS group cited LUTS to be the cause. Whereas those without LUTS cited various reasons like age, religious beliefs, various

The Massachusetts Male Aging Study observed that there was an association of sexual dysfunction with smoking in addition to other risk factors, like hypertension, diabetes mellitus and coronary artery disease (53). A similar association between sexual dysfunction with comorbid conditions and substance abuse was not seen in our study. This may be due to the fact that this study was not powered to study such an association.

The multinational survey of the aging male-7 (1) study, using the response to ,DAN-PSS questionnaire showed that erectile dysfunction was strongly associated with the severity of lower urinary tract symptoms($p < 0.001$). Our study also showed that the erectile dysfunction had an inverse relation with the severity of lower urinary tract symptom. It showed that the incidence of erectile dysfunction was significantly high amongst those with higher IPSS score in the age group 60 – 70 years ($p=0.02$). Both Similar results were also seen by other studies that reported a higher incidence of erectile and ejaculatory problems in men with moderate-to-severe LUTS (47).

Interestingly our study found that the average serum testosterone level in men more than 50 years was found to be 384 ± 159 ng/dl as compared to 437.8 ± 180.1 ng/dl in Americans, as in the study by Araujo AB et al (54)

Association between LUTS and ED in population based studies:

Year/Author	Name of study	Sample size	Assessment	Prevalence	Association
1994, Feldman et al (25)	MMAS	1709 (40-70yrs)	Structured interview of LUTS and ED	ED:52% (severe LUTS-66%)	ED: age, hypertension, depression, LUTS, medicines
1999, Lauman et al (55)	NHSS	1410 (18-59yrs)	Self reports of LUTS 1 question on ED	SD:31% ED:10%	ED - LUTS (odds ratio-3.13)
2001, Blaker et al (22)	Krimpen survey	1688 (30 – 80 yrs)	IPSS 4 ICS-sex question	ED: 11% EjD: 13%	ED: LUTS, age, smoking , CVS and pulmonary problem ED – LUTS Odds Ratio 7.5
2000, Braun et al (56)	Cologne male survey	4477 (30-80 yrs)	IPSS 18 KEED questions	LUTS: 44% ED: 19%	ED: LUTS, DM, hypertension, Pelvic surgery
2005, Li et al (57)	Asian Survey of Aging Males	(50-80 yrs) 1155	IPSS DAN-PSS-sex IIEF	ED: 63%(57% - bothered)	ED: age, LUTS, DM, hypertension ED : LUTS Odds ratio :3.17
2010, Holden et al, (58)	Australian male (telephonic survey)	(>40 yrs) 5990	IPSS single question of ED	LUTS : 16% ED: 21% ED/LUTS prostate related disease & androgen deficiency: 34%	ED : DM, Cardiovascular disease LUTS : Hypertension
2003, Rosen et al (1)	(USA/Europe) Multinational Survey of Aging Male	12,815 (50-80yrs)	IPSS DAN-PSS-sex IIEF	LUTS: 90% ED : 49%	ED and EjD: Severity of LUTS, age ED- LUTS Odds ratio 7.67
2013, Present study	Indian male	268 (>50 years)	IPSS IIEF	SD: 47% LUTS and no LUTS	SD: age, LUTS ED: severity of LUTS

Strengths

- a) 1st study in India showing the association of lower urinary tract symptoms with Sexual dysfunction in male more than 50 years of age
- b) Scales for the measurement of LUTS and Sexual dysfunction were internationally validated and standardized.
- c) Questionnaires were filled by the primary observer
- d) Association of sexual dysfunction with testosterone levels

Limitations

- a) Age was not matched, however a multivariate analysis was done to overcome this limitation
- b) The present study was not powered to study the associated risk factors for sexual dysfunction

Conclusions

- The prevalence of sexual dysfunction amongst men with LUTS was 47% whereas it was 24% in men without LUTS
- There is significant association of LUTS with sexual dysfunction in men >50 yrs, especially in the age group 50-70 yrs.
- LUTS had a significant impact on most of the domain of the IIEF 15.
- Severity of lower urinary tract symptoms correlated with the severity of erectile dysfunction in the age group 60-70 yrs.
- The mean testosterone in our study for males more than 50 years is 350ng/ml.
- LUTS was the reason for not being sexually active amongst the LUTS group.

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Annexure:

Proforma:

Name

Hospital number

Age

Occupation

Address

Phone number

(PLEASE TICK THE APPROPRIATE COLUMN)

Marital status

Married

Widower, separated, divorced.

Single

Promiscuous behaviour

Children

Sexually active

Socioeconomic status:

Govt. Service

Businessmen

Farmers/coolies (daily wagers)

Retired

Unemployed

Education

<10th

10+2

Graduate and above

Uneducated

Comorbid conditions

Diabetes

Hypertension

Heart disease

CKD

Depression (evaluated using PRIME MD questionnaire)

Smoking status :

Never

Former smoker

Current smoker

No. Of cigarettes per day

Alcoholic drinks

None

Yes

No. Of pegs per day

Physical activity

Less than average

Average

More than average

Previous surgeries:

(If yes mention the surgery-) -----

General Examination:

Pulse

BP

Weight

Height

BMI

External genitalia:

Pubic hair: (Tanners grade)

Testis size in cm (length x breadth)

Penis

Penile hygiene

Are you aware that ca penis is caused by bad penile hygiene

DRE (Digital rectal examination)

Laboratory Values:

RBS/AC/PC:

S. Creatinine:

Urine Microscopy:

Lipid profile:

Total cholesterol

Triglyceride

LDL

HDL

Serum testosterone:

X- ray KUB (kidney ureter bladder):

Uro flow and PVR (post void residue)

LUTS: IPSS (International prostate symptom score)

Absent or minor

Moderate

Severe

IIEF (International index of Erectile function)

Scoring Algorithm for IIEF

All items are scored in 5 domains as follows:

Domain	Items	Range	Score Max Score
Erectile Function	1, 2, 3, 4, 5, 15	0-5	30
Orgasmic Function	9, 10	0-5	10

Sexual Desire	11, 12	0-5	10
Intercourse Satisfaction	6, 7, 8	0-5	15
Overall Satisfaction	13, 14	0-5	10

Clinical Interpretation

I. Erectile function total scores can be interpreted as follows:

Score	Interpretation
0-6	Severe dysfunction
7-12	Moderate dysfunction
13-18	Mild to moderate dysfunction
19-24	Mild dysfunction
25-30	No dysfunction

1. Over the past 4 weeks, how often were you able to get an **erection** during sexual activity?

- ☐ No sexual activity
- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

2. Over the past 4 weeks, when you had **erections** with sexual stimulation, how often were your **erections** hard enough for penetration?

- ☐ No sexual stimulation
- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

Questions 3, 4 and 5 will ask about **erections** you may have had during sexual intercourse.

3. Over the past 4 weeks, when you attempted sexual intercourse, how often were you able to penetrate (enter) your partner?

- ☐ Did not attempt intercourse
- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

4. Over the past 4 weeks, during sexual intercourse, how often were you able to maintain your **erection** after you had penetrated (entered) your partner?

- ☐ Did not attempt intercourse
- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

5. Over the past 4 weeks, during sexual intercourse, how difficult was it to maintain your **erection** to completion of intercourse?

- ☐ Did not attempt intercourse
- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

6. Over the past 4 weeks, how many times have you attempted sexual intercourse?

- ☐ No attempts
- ☐ 1-2 attempts
- ☐ 3-4 attempts
- ☐ 5-6 attempts
- ☐ 7-10 attempts
- ☐ 11 or more attempts

7. Over the past 4 weeks, when you attempted sexual intercourse how often was it satisfactory for you?

- ☐ Did not attempt intercourse
- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

8. Over the past 4 weeks, how much have you enjoyed sexual intercourse?

- ☐ No intercourse
- ☐ Very highly enjoyable
- ☐ Highly enjoyable
- ☐ Fairly enjoyable
- ☐ Not very enjoyable
- ☐ Not enjoyable

9. Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you ejaculate?

- ☐ Did not attempt intercourse
- ☐ Almost always or always
- ☐ Most times (more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

10. Over the past 4 weeks, when you had sexual stimulation or intercourse how often did you have the feeling of orgasm or climax (with or without ejaculation)?

- ☐ No sexual stimulation or intercourse
- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

Questions 11 and 12 ask about sexual desire. Let's define sexual desire as a feeling that may include wanting to have a sexual experience (for example, masturbation or intercourse), thinking about having sex or feeling frustrated due to a lack of sex.

11. Over the past 4 weeks, how often have you felt sexual desire?

- ☐ Almost always or always
- ☐ Most times (much more than half the time)
- ☐ Sometimes (about half the time)
- ☐ A few times (much less than half the time)
- ☐ Almost never or never

12. Over the past 4 weeks, how would you rate your level of sexual desire?

- ☐ Very high
- ☐ High
- ☐ Moderate
- ☐ Low
- ☐ Very low or none at all

13. Over the past 4 weeks, how satisfied have you been with your overall sex life?

- 0 Very satisfied
- 0 Moderately satisfied
- 0 About equally satisfied and dissatisfied
- 0 Moderately dissatisfied
- 0 Very dissatisfied

14. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner?

- 0 Very satisfied
- 0 Moderately satisfied
- 0 About equally satisfied and dissatisfied
- 0 Moderately dissatisfied
- 0 Very dissatisfied

15. Over the past 4 weeks, how do you rate your confidence that you can get and keep your **erection**?

- 0 Very high
- 0 High
- 0 Moderate
- 0 Low
- 0 Very low

Scoring Algorithm for IIEF

All items are scored in 5 domains as follows:

Domain	Items	Range	Score Max Score
Erectile Function	1, 2, 3, 4, 5, 15	0-5	30
Orgasmic Function	9, 10	0-5	10
Sexual Desire	11, 12	0-5	10
Intercourse Satisfaction	6, 7, 8	0-5	15
Overall Satisfaction	13, 14	0-5	10

Clinical Interpretation

I. Erectile function total scores can be interpreted as follows:

Score	Interpretation
0-6	Severe dysfunction
7-12	Moderate dysfunction
13-18	Mild to moderate dysfunction
19-24	Mild dysfunction

25-30

No dysfunction

International Prostate Symptom Score (I-PSS)

Patient Name: _____ Date of birth: _____ Date completed: _____

In the past month:	Not at All	Less than 1 in 5 Times	Less than Half the Time	About Half the Time	More than Half the Time	Almost Always	Your score
1. Incomplete Emptying How often have you had the sensation of not emptying your bladder?	0	1	2	3	4	5	
2. Frequency How often have you had to urinate less than every two hours?	0	1	2	3	4	5	
3. Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Urgency How often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Weak Stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Straining How often have you had to strain to start urination?	0	1	2	3	4	5	
	None	1 Time	2 Times	3 Times	4 Times	5 Times	
7. Nocturia How many times did you typically get up at night to urinate?	0	1	2	3	4	5	
Total I-PSS Score							

Score: 1-7: Mild 8-19: Moderate 20-35: Severe

Quality of Life Due to Urinary Symptoms	Delighted	Pleased	Mostly Satisfied	Mixed	Mostly Dissatisfied	Unhappy	Terrible
If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?	0	1	2	3	4	5	6

About the I-PSS

The International Prostate Symptom Score (I-PSS) is based on the answers to seven questions concerning urinary symptoms and one question concerning quality of life. Each question concerning urinary symptoms allows the patient to choose one out of six answers indicating increasing severity of the particular symptom. The answers are assigned points from 0 to 5. The total score can therefore range from 0 to 35 (asymptomatic to very symptomatic).

The questions refer to the following urinary symptoms:

Questions	Symptom
1	Incomplete emptying
2	Frequency
3	Intermittency
4	Urgency
5	Weak Stream
6	Straining
7	Nocturia

Question eight refers to the patient's perceived quality of life.

The first seven questions of the I-PSS are identical to the questions appearing on the American Urological Association (AUA) Symptom Index which currently categorizes symptoms as follows:

Mild (symptom score less than or equal to 7)
Moderate (symptom score range 8-19)
Severe (symptom score range 20-35)

The International Scientific Committee (SCI), under the patronage of the World Health Organization (WHO) and the International Union Against Cancer (UICC), recommends the use of only a single question to assess the quality of life. The answers to this question range from "delighted" to "terrible" or 0 to 6. Although this single question may or may not capture the global impact of benign prostatic hyperplasia (BPH) Symptoms or quality of life, it may serve as a valuable starting point for a doctor-patient conversation.

The SCI has agreed to use the symptom index for BPH, which has been developed by the AUA Measurement Committee, as the official worldwide symptoms assessment tool for patients suffering from prostatism.

The SCI recommends that physicians consider the following components for a basic diagnostic workup: history; physical exam; appropriate labs, such as U/A, creatine, etc.; and DRE or other evaluation to rule out prostate cancer.

PHQ-9 Depression

**Over the last 2 weeks, how often have you
been bothered by any of the following problems?**

(Use “✓” to indicate your answer”

	Not all	at Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things.....	0	1	2	3
2. Feeling down, depressed, or hopeless.....	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much.....	0	1	2	3
4. Feeling tired or having little energy.....	0	1	2	3
5. Poor appetite or overeating.....	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down.....	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television.....	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual.....	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way.....	0	1	2	3

Column totals ____ + ____ + ____ + ____

= Total Score ____

From the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MD PHQ). The PHQ was developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues. For research information, contact Dr. Spitzer at rls8@columbia.edu. PRIME-MD® is a trademark of Pfizer Inc. Copyright© 1999 Pfizer Inc. All rights reserved. Reproduced with permission

Scoring notes.

- **PHQ-9 Depression Severity**

Scores represent: **0-5 = mild 6-10 = moderate 11-15 = moderately severe**
16-20 = severe depression

- **GAD-7 Anxiety Severity.**

This is calculated by assigning scores of 0, 1, 2, and 3, to the response categories of “not at all,” “several days,” “more than half the days,” and “nearly every day,” respectively. GAD-7 total score for the seven items ranges from 0 to 21.

Scores represent: **0-5 mild 6-10 moderate 11-15 moderately severe anxiety**
15-21 severe anxiety.

- **Core-10**

Key points in the scoring of the CORE-10 are as follows:

1. Each item within the CORE-10 is scored on a 5-point scale ranging from 0 ('not at all') to 4 ('most or all the time').
2. The clinical score is calculated by adding the response values of all 10 items.
3. Where there are missing data the clinical score is derived by calculating the total mean score (dividing the total score by the number of completed items) and multiplying by 10.
4. We do not recommend re-scaling the clinical score if more than one item is missing.
5. The minimum score that can be achieved is 0 and the maximum is 40.
6. The measure is problem scored, that is, the higher the score the more problems the individual is reporting and/or the more distressed they are.

A score of 10 or below denotes a score within the non-clinical range and of 11 or above within the clinical range. Within the non-clinical range we have identified two bands called 'healthy' and 'low' level distress. People may score on a number of items at any particular time but still remain 'healthy'. Similarly, people may score in the 'low' range which might be a result of raised pressures or particular circumstances but which is still within a non-clinical range. **Within the clinical range we have identified the score of 11 as the lower boundary of the 'mild' level, 15 for the 'moderate' level, and 20 for the 'moderate-to-severe' level. A score of 25 or over marks the 'severe' level.**